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Monograph

MONOGRAPH

Nonmedical Cannabis Use: Patterns and Correlates of Use, Exposure, and Harm, and Cancer Risk

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Abstract

Cannabis has certain health benefits, but some people may experience harms from use. Co-use of tobacco and cannabis is common. Smoke from cannabis contains many of the same carcinogens and toxicants as the smoke from tobacco, raising concerns that cannabis smoking may be a risk factor for cancer. With growing access to and acceptance of medical and nonmedical cannabis, there is an urgent need to understand the risks and benefits of the current modes of cannabis use and how cannabis may be associated with cancer risk. This monograph summarizes a session from a National Cancer Institute Symposium on nonmedical cannabis use and cancer risk. We had 3 objectives: describe the relation between nonmedical cannabis use and cancer risk, delineate patterns and correlates of cannabis co-use with tobacco, and document potentially harmful inhalational exposure resulting from smoked and vaped cannabis. Methodological limitations in the literature and future research recommendations are provided.

Even though cannabis remains illegal at the federal level as a Schedule I drug, more than one-half of US states now allow for recreational, medical, and/or decriminalized use of cannabis. According to US Census data, the majority of Americans live in a state with some form of legalized cannabis use, and nearly 110 million live in a state with legalized recreational use, accounting for roughly 33% of the current US population (1). Cannabidiol and hemp oil products are now legal across the United States, including product versions that are smoked and vaped. There is limited regulation of the marketplace for these emerging products. Not surprisingly, the US population's interest in and use of cannabis to alleviate or treat certain medical conditions has increased in the last decade. Medical cannabis use has potential positive utility, including for the treatment of cancer-related symptoms and side effects from cancer treatment. Trials of medical cannabis products suggest that cannabis could have therapeutic benefits in the management of pain and nausea, both of which are symptoms resulting from cancer and chemotherapy (2,3). Among adults seeking a medical cannabis card, 87% said they were seeking a card to address pain (2). Inadequately treated pain, difficulty obtaining pain medication (eg, lack of insurance or insurance coverage for specific medications), concern about prescription pain medication side effects, and the addiction potential of pain medications are motivators to use cannabis. More than 75% of health provider respondents to a *New England Journal of Medicine* poll said that they would recommend the use of cannabis for pain and nausea despite the fact that it was illegal in most parts of the United States (4). Studies have shown reductions in prescription drug use and opioid use following state implementation of legal medical cannabis (5–7). This suggests a potential positive health impact of allowing individuals to treat their ailments with cannabis as opposed to other prescription drugs.

Although there are noted benefits of cannabis use for certain health conditions (3), some users may experience harms associated with use. Across all age groups, there is strong evidence

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that both short- and long-term cannabis use is associated with mental and physical health problems, such as increased risk of frequent and chronic respiratory problems and impairments in cognition and memory (3). Cannabis is also frequently used together ("co-used") with other substances of abuse (8–10), and this co-use is correlated with greater substance dependence (11,12), poor tobacco and cannabis cessation outcomes (13,14), increased exposure to harmful chemicals (15–17), and increased cancer risk (18–21). Co-use of tobacco and cannabis is increasingly common (22) and is associated with greater exposure to harmful smoke chemicals (23), which may be particularly relevant to cancer risk and health outcomes.

With growing access to and acceptance of medical and recreational cannabis, there is an urgent need to understand the risks and benefits of cannabis use and how cannabis use might intersect with cancer risk and treatment so that patients and providers are able to make informed treatment decisions. This monograph summarizes a session on nonmedical cannabis use and cancer epidemiology from the "NCI Cannabis, Cannabinoids, and Cancer Research Symposium" held in December 2020, with a focus on nonmedical cannabis use (eg, cannabis that is used for recreational rather than medical purposes) and cancer epidemiology in 3 overlapping areas: 1) current evidence on cannabis use and cancer risk, 2) patterns and correlates of cannabis use and tobacco co-use, and 3) potentially harmful inhalational exposure resulting from smoked and vaped cannabis.

Cannabis and Cancer Risk: Current Evidence and Methodological Considerations

Smoke from cannabis contains several of the same carcinogens as tar from tobacco (15), raising concerns that it may be a risk factor for cancer. We previously reviewed studies on cannabis and cancer risk for epidemiologic studies published through August 2014 (19). We searched for new epidemiologic studies published up to November 2020 on cannabis use and cancer risk with a PubMed search on keywords including "cannabis" or "marijuana" and "cancer." Studies that did not report odds ratios or risk ratios were excluded. Results from almost 40 epidemiological studies were identified on cannabis smoking and the risk of cancer. We reviewed the epidemiological studies in terms of the strength of association, consistency, temporality, and biological gradient (24). Cancers assessed in the epidemiological studies cited below include upper aerodigestive tract (UADT), lung, testicular, and childhood cancers. For smoking-related cancers, odds ratios adjusted for tobacco smoking were cited unless otherwise noted.

UADT Cancers

Cannabis use and UADT cancer risk have been investigated in 10 case-control studies and 2 pooled-data analyses (see Table 1). Head and neck cancers include oral cavity, oropharynx, hypopharynx, and larynx, and UADT cancers include oral cavity, oropharynx, hypopharynx, and larynx + esophagus. The number of participants in 5 hospital-based case-control studies ranged from 53 to 636 for 1 study in New York, 2 in the United Kingdom, 1 in Baltimore, and 1 in North Africa (25–29). The studies in New York and Baltimore reported statistically significant associations between cannabis use and head and neck cancer risk (25,28). The New York study estimated an odds ratio of 2.6 (95% confidence interval [CI] = 1.1 to 6.6) and statistically significant P values for dose-response relations for the frequency and duration of cannabis use with head and neck cancer risk (25). In the Baltimore study, human papilloma virus (HPV) 16+ patients had statistically significant increased risk for head and neck cancer for cannabis use (odds ratio = 4.7, 95% CI = 1.3 to 17) as well as statistically significant dose-response relations for the frequency and duration of cannabis use, but no statistically significant odds ratios, frequency, or duration for HPV16− patients (28). The North African study did not identify an association between cannabis use and the risk of nasopharyngeal cancer; however, a dose response for cumulative cannabis use and nasopharyngeal cancer risk was suggested ($P = .02$) (29).

In terms of population-based case-control studies of UADT cancer, 5 were conducted at multiple centers in the United States as well as in Washington state, Los Angeles, Boston, and New Zealand (30–34). The participants in these studies ranged from 70 sinonasal cancer cases to 434 head and neck cancer cases. Associations between cannabis use and UADT cancers were not observed in the population-based studies.

For the pooled-data studies, J. Berthiller et al. (35) pooled studies from Seattle, Tampa, Los Angeles, Houston, and Latin America, with 4029 cases and 5015 controls. There was no association between cannabis use and head and neck cancer risk, and no dose response identified for frequency, duration, or cumulative exposure. M.A. Marks et al. (36) used the data from the Berthiller study and additionally pooled studies from Baltimore, Boston, Seattle, and North Carolina, with 1921 oropharyngeal cancer cases and 356 oral tongue cancer cases. A statistically significant odds ratio of 1.24 (95% CI = 1.06 to 1.47) was reported for cannabis use and oropharyngeal cancer risk. On the other hand, there was a decreased risk for tongue cancer with an odds ratio of 0.47 (95% CI = 0.29 to 0.75), with dose-response relations identified for both frequency and duration.

The pooled analyses included studies that had not been published, perhaps because the results for those studies did not identify clear associations. The 3 studies investigating HPV and cannabis use on the risk of head and neck cancer suggest that HPV may be a modifying factor.

In summary, case-control studies on UADT cancers identified increased and decreased risks, possibly because risks differ by HPV status, head and neck cancer subsites, or geographic location.

Lung Cancer

For lung cancer, there were 4 case-control studies: 2 in Tunisia, 1 in Los Angeles, and 1 in New Zealand (see Table 2) (32,37–39). The Tunisia studies reported very strong odds ratios of 8.2 (95% CI = 1.3 to 15.5) and 2.4 (95% CI = 1.6 to 3.8), respectively (37,38). In the population-based Los Angeles study, although a decreased odds ratio was observed in the lower joint-year category (0.44, 95% CI = 0.21 to 0.92), there was no association between cannabis use and the risk of lung cancer for higher joint-years of use (32). A joint-year is equivalent to smoking 1 joint per day for 1 year. The New Zealand study reported a very modest increase in risk of 1.08 (95% CI = 1.02 to 1.15), with dose-response relations observed for the frequency of cannabis use (39).

There were also 2 cohorts and 1 pooled study for cannabis use and the risk of lung cancer (40,41). The cohorts from Sweden and California did not suggest any association between cannabis smoking and lung cancer risk. The pooled study included studies from the United States, Canada, the United

Table 1 Epidemiological studies on cannabis use and the risk of upper aerodigestive tract cancers[a]

First author	Location, y	Cases	Controls	Odds ratio (95% CI) for cannabis use	Dose response
Hospital-based studies					
Zhang (25)	New York, 1992-1994	173 UADT	176 blood donors	2.6 (1.1 to 6.6)	Frequency: $P = .0214$ Duration: $P = .0134$
Llewellyn (26)	United Kingdom, 1990-1997	116 oral, oropharynx ≤45 y	207 controls from GP registers	1.0 (0.5 to 2.2)	Not reported
Llewellyn (27)	United Kingdom, 1999-2001	53 oral, oropharynx ≤45 y	91 controls from GP registers	0.3 (0.1 to 1.8)	Not reported
Gillison (28)	Baltimore, MD, 2000-2006	240 head and neck	322 hospital controls	HPV16+ patients: Current: 4.7 (1.3 to 17) HPV16− patients: 2.0 (0.62 to 6.5)	HPV16+ patients: Frequency: $P = .007$ Duration: $P = .001$
Feng (29)	North Africa, 2002-2005	636 nasopharyngeal	615 hospital controls	0.97 (0.37 to 2.52)	Frequency: $P = .10$ Cumulative: $P = .02$
Population-based studies					
Zhu (30)	United States, 1984-1988	70 sinonasal 113 nasopharynx Men only	1910 population controls	Sino: 1.3 (0.6 to 2.7) Naso: 0.2 (0.1 to 0.4) *Not adjusted for tobacco	Not assessed
Rosenblatt (31)	Washington state, 1985-1995	407 oral	615 population controls	0.9 (0.6 to 1.3)	No dose response
Hashibe (32)	Los Angeles, CA, 1999-2004	303 oral 100 pharynx 90 larynx	1040 population controls	Oral: 0.93 (0.53 to 1.60) Ph: 0.92 (0.41 to 2.10) La: 1.20 (0.26 to 5.50)	Estimates are for never smokers; No dose response
Liang (33)	Boston, MA, 1999-2003	434 head and neck	547 population controls	0.48 (0.22 to 1.06)	No dose response for cumulative smoking
Aldington (34)	New Zealand, 2001-2005	75 UADT <55 y	319 population controls	1.0 (0.5 to 2.3)	No dose response for joint-years
Pooled-data studies					
Berthiller (35)	Seattle, Tampa, Los Angeles, Houston, Latin America	4029 head and neck	5015 controls	0.88 (0.67 to 1.16)	No dose response identified for frequency, duration, or cumulative exposure
Marks (36)	Berthiller studies + Baltimore, Boston, Seattle, and North Carolina	1921 oropharyngeal cancer 365 oral tongue	7639 controls 4321 controls	Oropharynx: 1.24 (1.06 to 1.47) Tongue: 0.47 (0.29 to 0.75)	Dose response for frequency and duration for both oropharyngeal cancer and tongue cancer

[a]CI = confidence interval; GP = general practitioner; HPV = human papilloma virus; UADT = upper aerodigestive tract.

Table 2. Epidemiological studies on cannabis use and the risk of lung cancer[a]

First author	Location, y	Cases	Controls or cohort	Odds ratio (95% CI)	Dose response
Case-control studies					
Hsairi (37)	Tunisia, 1988-1989	110 cases	110 residents	8.2 (1.3 to 15.5)	Not reported
Berthiller (38)	Tunisia, 1996-2004	430 cases	755 hospital-based controls	2.4 (1.5 to 3.7)	No dose response for frequency or duration
Hashibe (32)	Los Angeles, 1999-2004	611 cases	1040 population controls	• ≥0 to 1 joint-years: 0.44 (0.21 to 0.92) • ≥1 joint years: 1.1 (0.48 to 2.6)	No dose response
Aldington (39)	New Zealand, 2001-2005	79 cases	324 controls from district health boards	For ever joint-year increase, RR = 1.08 (1.02 to 1.15)	Dose-response for frequency; duration of use not assessed
Cohort studies					
Callaghan (40)	Sweden, 1969-2009	179 cases	49 321 young men ages 18-20 in military	1.25 (0.84 to 1.87)	Dose-response for frequency suggested; duration of use not assessed
Sidney (41)	California, 1979-1993	49 cases	1421 cases	• Men: 0.9 (0.5–1.7) • Women: 1.1 (0.5 to 2.6)	
Pooled-data study					
Zhang (18)	United States, Canada, United Kingdom, and New Zealand	2159 cases	2985 controls	1.03 (0.51 to 2.08)	Estimates are for never tobacco smokers; dose response not observed for joint-years

[a]CI = confidence interval; RR = XXX.

Kingdom, and New Zealand and did not show any association between cannabis smoking and lung cancer risk (18).

Overall, the North African studies reported increased risk; however, tobacco is commonly mixed with cannabis in the region, thus making it difficult to rule out residual confounding by tobacco smoking. The highest exposure ranged from greater than 50 times of use over a lifetime (1 joint/wk for a year), 1-2 joint-years (1-2 joints/d for a year), or greater than 10 joint-years. Even 10 joint-years would translate into 0.5 pack-years of cigarette smoking, with the assumption that 1 joint is similar to 1 cigarette. In most studies of cigarette smoking, such cumulative exposure would be classified as never smoker, because ever smokers are often defined as having smoked 100 cigarettes over a lifetime.

In summary, the results from the lung cancer studies largely appear to not support an association with cannabis use, possibly due to the smaller amounts of cannabis regularly smoked by study participants compared with tobacco. The lack of associations in some of the UADT cancer studies may also be subject to the issue of smaller amounts of cannabis regularly smoked.

Testicular Cancer

For testicular cancer, there were 3 case-control and 1 cohort study on cannabis use and cancer risk (see Table 3). The case-control studies were from Washington state (42); at multiple sites in Texas, Louisiana, Arkansas, and Oklahoma (43); and Los Angeles (44). These studies were a mix of hospital-based and population-based study designs. The Washington state study reported a twofold increase in risk for daily cannabis use and similar levels of risk whether cannabis was used for less than 10 years or 10 or more years (42). The second study showed a protective effect for using less than 1 time per day and an increased risk for daily or greater than daily use (43). The Los Angeles study showed a twofold increased risk for the lower frequency and duration categories of cannabis use (<1/wk and <10 years) but no increased risk for over 1/wk or over 10 years of cannabis use (44). The Swedish cohort included 49 343 men, 18-20 years of age, in the military and showed no association, except for over the 50 times of cannabis use, with an odds ratio of 2.57 (95% CI = 1.02 to 6.50) (45). Although the 3 case-control studies investigated testicular cancer risk by frequency and duration of cannabis use, none showed strong dose-response relations. In summary, 4 testicular cancer studies reported increased risks with cannabis use, but dose-response trends were not established.

Childhood and Other Cancers

For childhood leukemia, there were 3 case-control studies that investigated cannabis use in the parent and the risk of leukemia in the child (see Table 4) (46–48). For the first study, the odds radio was very high at 11.0 (95% CI = 1.42 to 85.20) for maternal use of mind-altering drugs (9 out of 11 patients used cannabis); however, no association was observed with paternal use (46). The second study reported a 1.5-fold increase in risk for ever use by the father ($P < .05$) (47). For the third study, maternal use was not associated with cancer; however, there was an increased risk for paternal ever use (odds ratio = 1.37, 95% CI = 1.02 to 1.83) (48).

Table 3. Epidemiological studies on cannabis use and the risk of testicular cancer[a]

Author	Study location, period	Cases	Controls or cohort	Frequency Odds ratio (95% CI)	Duration Odds ratio (95% CI)
Daling (42)	Washington State, 1999-2006	369 cases aged 18-44 y	979 population controls	• <1/wk = 1.4 (0.9 to 2.3) • Daily or ≥1 d/wk = 2.0 (1.3 to 3.2)	• <10 y = 1.8 (1.0 to 3.3) • ≥10 y = 1.6 (1.1 to 2.5)
Trabert (43)	Texas, Louisiana, Arkansas, Oklahoma, 1990-1996	187 cases aged 18-50 y	148 hospital controls	• Never = 1.0 • <1/d = 0.5 (0.3 to 0.9) • Daily or >1/d = 2.2 (1.0 to 5.1)	• <10 y = 0.6 (0.3 to 1.0) • ≥10 y = 1.2 (0.6 to 2.8)
Lacson (44)	Los Angeles, CA, 1986-1991	163 cases aged 18-35 y	292 controls	• <1/wk = 2.10 (1.09 to 4.03) • ≥1/wk = 1.53 (0.73 to 3.24)	• <10 y = 2.09 (1.09 to 3.98) • ≥10 y = 1.51 (0.66 to 3.47)
Callaghan (45)	Sweden, 1970-2011	119 cases	Cohort of 49 343 men, aged 18-20 y in military	Ever cannabis smoking • Never • 1-4 times • 5-10 times • 11-50 times • >50 times	• 1.42 (0.83 to 2.45) • 1.0 • 0.95 (0.41 to 2.19) • 2.15 (0.77 to 5.95) • 1.17 (0.28 to 4.85) • 2.57 (1.02 to 6.50)

[a]CI = confidence interval.

Table 4. Epidemiological studies on cannabis use and the risk of childhood cancer [a]

Author	Study location, period	Cases	Controls	Exposure categories	Odds ratio (95% CI)
Robison (46)	Multiple United States and Canada, 1980-1984	204 childhood acute nonlymphoblastic leukemia cases	204 patients	• Maternal use of mind-altering drugs (9/11 patients used cannabis) • Paternal use	• 11.0 (1.42 to 85.20) • 1.47, $P = .32$
Wen (47)	Multiple United States, Canada, and Australia, 1983-1993	1805 acute lymphoblastic leukemia cases, 528 acute myeloid leukemia	2723 patients	Ever cannabis use by father	1.5 ($P < .05$)
Trivers (48)	Multiple United States and Canada, 1989-1993	638 childhood acute myeloid leukemia cases	610 matched controls	• Maternal ever use • Paternal ever use	• 0.89 (0.66 to 1.19) • 1.37 (1.02 to 1.83)
Kuijten (49)	Pennsylvania, New Jersey, Delaware, and United States, 1980-1986	163 childhood astrocytoma cases	163 patients	Gestational cannabis exposure	2.8 (0.9 to 9.9)
Grufferman (50)	Multiple United States, 1982–1988	322 childhood rhabdomyosarcoma cases	322 patients	• Maternal use of cannabis • Paternal use	• 3.0 (1.4 to 6.5) • 2.0 (1.3 to 3.3)
Bluhm (51)	Multiple North America, 1992-1994	538 childhood neuroblastoma cases	504 age-matched controls	Maternal use frequency in first trimester • <1 pipeful/d • ≥1 pipeful/d	• 1.37 (0.77 to 2.49) • 4.16 (1.52 to 14.61) • 4.42 (1.09 to 29.58)

[a]CI = confidence interval.

For other childhood cancers, there were 3 case-control studies on cannabis use by parents (49–51). For the multicenter study in Pennsylvania, New Jersey, and Delaware, there was no association with use during the gestational period for astrocytoma (49). For a US multicenter study, there was a threefold increased rhabdomyosarcoma risk for maternal use and a twofold increased risk for paternal use (50). Another multicenter study in North America estimated a fourfold increased risk for less than 1 pipeful per day and for 1 or more pipefuls per day in the first trimester for neuroblastoma risk (51).

The childhood cancer studies shared limitations, such as small numbers of exposed cases, possible exposure misclassification due to recall bias, and no dose-response assessment. The studies' strengths included large sample sizes and information on the use of specific recreational drugs within specific time periods relative to pregnancy or birth .

A Kaiser Permanente cohort studied multiple cancers and reported that cannabis use was associated with increased risks of prostate and cervical cancers, but not colorectal, melanoma, or breast cancers (41). There was no association for anal, penile, or non-Hodgkin's lymphoma (52–54). Two other studies on non-Hodgkin's lymphoma and bladder cancer reported decreased cancer risks (55–57).

For childhood cancers and other cancer sites, there are still insufficient data to make conclusions on an association with cannabis smoking, although a few studies on non-Hodgkin's Lymphoma and bladder cancer have reported potential protective effects.

Methodological Issues

Some methodological issues for the epidemiological studies of cannabis use and cancer risk included possible underreporting by participants due to the illegality of cannabis use when and where the study took place, small sample sizes, and too few heavy cannabis users identified, which may change with legalization. Additionally, confounding by tobacco smoking makes the effect of cannabis difficult to disentangle. Possible solutions include restricting studies to nonsmokers and adjusting for tobacco smoking statistically. Appropriate adjustment requires many tobacco variables (eg, never, current, or past use; frequency; duration; years since quitting). Types of tobacco used also need to be considered (eg, cigarettes, cigars, pipes, vaping). Previous studies usually did not collect that level of detail for tobacco variables.

Gaps in previous research include a focus on smoked cannabis and a lack of data on other types of cannabis, such as vaping and edibles; few cohort studies that are prospective in design, which would minimize recall bias; lack of use of biological markers in combination with self-reported measures of cannabis use; and not fully leveraging pooled data in epidemiological consortia. Pooled data allow for larger sample sizes and a focus on specific subgroups. New well-designed epidemiological studies on cannabis use and risk of cancer are needed.

Conclusion

For cancer risk, although there are 40 published epidemiological studies, the results have not been consistent on an association between plant-based smoked cannabis and cancer risk. Because cannabis use patterns are changing now with legalization and various product availability, new well-designed studies are needed to investigate cancer risk with current modes of cannabis use. Including cannabis exposure biomarkers would enhance the epidemiological studies. Considering the complexity of cannabis and tobacco co-use and various modes of use will be important in any new studies.

Cannabis and Tobacco Co-Use: Patterns, Correlates, and Implications for Reducing Cancer Risk

This section will review the state of the science on cannabis and tobacco co-use, including common definitions of co-use and modes of administration, patterns and correlates of co-use behavior, and the role of the tobacco industry and the cannabis industry in influencing use behavior. Because co-use is predominant among younger users, most studies, understandably, have focused on younger age groups, who are less likely to show acute cancer risk. More work is needed among specific subgroups with high rates of cancer to understand the correlates of co-use and cancer-related health consequences.

Definitions of Cannabis and Tobacco Co-Use

There are several methods by which cannabis and tobacco can be co-used. A joint refers to cannabis wrapped in rolling paper, not tobacco paper, and does not contain tobacco. Joints are considered one of the most common forms of combusted cannabis. A spliff is similar to a joint, except that tobacco is added. Some users state that the benefits of spliff smoking include that it is easier to roll than a joint because the tobacco provides structure, the tobacco in the spliff masks the potentially strong odor of combusted cannabis, and the product burns more smoothly and evenly than a joint. A blunt refers to removing all or part of the tobacco from a cigar and replacing it with cannabis. Noted benefits among blunt users are that blunts are large so they can be used in a group setting; they increase one's high; they come in flavors, unlike smoking a joint; and the thick tobacco paper of the cigar allows for a slower burn. Vaping cannabis refers to vaporizing (eg, heating but not burning) the flower or the loose-leaf form of cannabis or concentrates, such as tetrahydrocannabinol (THC, the main psychoactive chemical in cannabis) oils or wax in a variety of vaping devices. Lastly, smoking cannabis through a hookah or waterpipe refers to combining the flower of loose-leaf cannabis or oils or concentrates with shisha in a hookah or waterpipe. Shisha contains tobacco and is placed in the bowl of the hookah or waterpipe and can also be flavored or unflavored (eg, traditional tobacco flavor). The use of multiple hoses allows for sharing and a more social experience.

In addition to different modes of cannabis and tobacco co-use ingestion, there are also several definitions of co-use. Combined use describes the use of cannabis and tobacco within the same product, such as in a blunt or a spliff. Simultaneous use is the co-use of cannabis and tobacco during the same episode, but not necessarily combined. For example, chasing refers to using tobacco after using cannabis. Lastly, concurrent use refers to the use of cannabis and tobacco on separate occasions but within the same time period, such as in the past 30 days or past year.

Why Focus on Co-Use in Relation to Cancer?

There are a number of reasons why the topic of cannabis and tobacco use is relevant to cancer risk. First, tobacco use is quite high among co-users. A population-based study conducted in the U.S. using the National Survey of Drug Use and Health (NSDUH) found showed that 68% of past-month cannabis users reported tobacco use in the past month; while while rates of past-month tobacco use among non-cannabis users was much lower, at 25.30%. These numbers are staggeringly high and

concerning given the known links among combustible tobacco use, exposure to cancer-causing carcinogens, and cancer. Second, beyond tobacco use, there are a variety of health and psychological consequences associated with co-use. Co-use of cannabis and tobacco is correlated with greater cannabis and nicotine dependence (11,12,58), poor tobacco cessation and cannabis outcomes (13,14), increased cancer risk (18–21), alcohol and other drug use (8–10), anxiety and depression (59–62), and increased risk of health behaviors associated with cancer, such as certain respiratory problems (3).Third, there are health disparities and hidden risks associated with co-use that are important to consider with respect to cancer risk.

As you will be shown later in this section, the demographics of co-users are similar to those who show cancer-related health disparities; these include lower socioeconomic status, certain racial or ethnic minority groups, and mental or physical health problems. There are also several "hidden" risks associated with co-use that the public may not be aware of or think about, including firsthand and secondhand smoke exposure from cannabis use. For example, many of the same constituents in tobacco smoke are found in cannabis smoke (15). In terms of secondhand smoke exposure, 1 recent study found that almost 27% of US adults reported indoor and outdoor exposure to cannabis secondhand smoke in the past 7 days (63). Also, co-users misperceive harm associated with their use. The rapidly changing policies surrounding cannabis's legal use has been correlated with decreased perceptions of cannabis-related harm over the last decade, and lower harm perceptions of cannabis use are correlated with more frequent and intense use and predict future intentions to use cannabis (64–66). Furthermore, even though the tobacco is removed from a blunt, research shows that the cigar wrapper used for blunt smoking contains nicotine (67), furthering the cycle of tobacco use. Finally, there is a "double whammy" of smoked or combusted tobacco with combusted cannabis. Exposure to both of these combusted products at the same time may increase exposure to cancer-causing carcinogens. There is only nascent work in this area with humans.

Patterns of Cannabis and Tobacco Co-Use and Tobacco Product Popularity

The United States has seen tremendous declines in cigarette smoking among adults and youth for the past several decades (68). However, this is not the entire picture. The use of noncigarette tobacco products, such as e-cigarettes, hookah or shisha, and cigar products (eg, large cigars, little cigars or cigarillos [LCC]), has increased over this time among both youth and adults. Most of these products are co-used with cannabis and come in a variety of characterizing sweet and savory flavors (eg, chocolate, fruit, alcohol, mint or menthol), which may further enhance their appeal (69,70).

The prevalence of cannabis and tobacco co-use has increased over time, particularly among young adults (ages 18-24 years) (71). In a seminal study using 2003-2012 data from the National Survey on Drug Use and Health, approximately 5.20% of the US adult population reported past-month co-use, 24% reported tobacco-only use in the past month, and 2.3% reported cannabis-only use in the past month. To date, we are not aware of any published studies that have examined recent changes in co-use behavior that include blunt smoking, cannabis vaping, and combined cannabis co-use with hookah, waterpipe, or shisha tobacco.

A pilot analysis of data from Wave 4 (2017-2018) of the Population Assessment of Tobacco and Health (PATH) Study was conducted for this monograph to examine the current prevalence of co-use among the US population of youth (ages 12-17 years), young adults (ages 18-24 years), and older adults (age 25+ years) who reported using at least 1 of 10 different tobacco products in the past 30 days. We examined the relative rankings and differences in the past 30-day use of each of 10 different tobacco products (cigarettes, e-cigarettes, traditional cigars, cigarillos, filtered cigars, pipe, hookah, snus, smokeless, and dissolvable tobacco) across past 30-day co-users and tobacco-only users (of any combination of tobacco products). Snus is a moist or loose-leaf smokeless form of tobacco that can be packaged in a pouch and placed underneath the lip.

PATH is a national longitudinal study designed to examine patterns and health effects of tobacco use in approximately 49 000 US youth and adults, collected annually since 2013. Details regarding the PATH Study design and methods have been published and can be found at Hyland et al (72). The analyses presented below are from a subset of n = youth (n = 3169) and adults (n = 15 185) who reported using at least 1 tobacco product in the past 30 days in Wave 4. Co-use for this analysis was defined as reporting past 30-day use of cannabis among current (eg, past 30 days) tobacco users.

Analysis of youth past-30-day tobacco users showed that 8.26% of past-30-day tobacco users reported past-30-day cannabis use. In terms of the popularity of individual tobacco products, cigarettes and e-cigarettes were the most popular products used across both youth co-users and tobacco-only users (cigarettes: 82.4% for co-users vs 79.23% for tobacco-only users; e-cigarettes: 22.94% for co-users vs 17.94% for tobacco-only users). Compared with tobacco-only users, a statistically significantly greater percentage of youth past-30-day cannabis and tobacco co-users reported past-30-day e-cigarette use ($P = .0193$). No other differences in the prevalence of tobacco product use between co-users and tobacco-only users were found. The sample for past-30-day blunt use among youth was too small to examine group differences.

Past-30-day cannabis and tobacco co-use among young adult tobacco users was nearly 5 times higher among young adult tobacco users compared with the youth past-30-day tobacco users. Nearly one-half (47.9%) of past-30-day young adult co-users reported co-use. Co-users reported a statistically significantly higher prevalence of cigarillo or filtered cigar smoking in the past 30 days compared with tobacco-only users (33.1% vs 24.57, $P < .001$). Compared with tobacco-only users, co-users reported a statistically significantly lower prevalence of smokeless tobacco (8.46% vs 13.80%, $P = .001$) and snus use (3.07% vs 5.41%, $P = .014$).

Almost one-third (27.07%) of adult (25 years and older) past-30-day tobacco users reported past-30-day co-use, which is statistically significantly lower than the prevalence of co-use among young adults. Cigarettes, again, remained the most popular tobacco product used in the past 30 days across both co-users and tobacco-only users (79.73% vs 79.59%, $P = .926$). With the exception of cigarettes, co-users reported a statistically significantly higher prevalence of combustible product use compared with tobacco-only users for all products assessed (all were $P < .001$).

In summary, our analysis of recent PATH data found that the rates of past 30-day co-use were highest among young adult past-30-day tobacco users and lowest among youth past-30-day tobacco users, aligning with the findings from previously published work using the National Survey on Drug Use and Health (71). Cigarettes were the most popular tobacco product used in the past 30 days among all ages of co-users; however, the rankings or

popularity of individual tobacco products beyond cigarettes differed across the age groups. Notably, cigars and blunts were highly popular among young adult co-users, which is concerning because smoking cigars confers similar cancer-related risk compared with smoking cigarettes (73) and, in some cases, greater exposure to toxins and cancer-causing carcinogens (74). We were unable to examine the prevalence of blunt smoking in the youth sample, given the small sample size, so we were unable to determine the popularity of this particular form of cannabis and tobacco co-use in this age group. Finally, combustible tobacco use was statistically significantly higher among older adult co-users (25 years and older) compared with older adult tobacco-only users. Thus, adult co-users may be exposed to greater cancer-causing carcinogens and toxins compared with tobacco-only users and appear to have the greatest exposure compared with youth and young adult co-users. An important methodological limitation of the PATH data is worth noting with respect to the measurement of cannabis use. Questions about cannabis use do not specify mode of ingestion (eg, combustible, edible, etc); thus, we are unable to tease apart combustible vs noncombustible forms of cannabis use and their relation to tobacco product use.

Demographic Correlates of Co-Use

Schauer et al. (71) conducted the most comprehensive population-level analysis to date of the demographic correlates of co-use of cannabis and tobacco products using data from the 2002-2012 National Survey on Drug Use and Health. Results from this study are reviewed below. Co-users were more likely to be Black or African American (16%) compared with tobacco-only users (11.1%), and co-use increased by 23% among Black or African American and 21.9% among Hispanic individuals over the 10-year period, which is a statistically significantly faster rate than for White respondents. It is important to note that these same demographics also overlap with those subgroups who have high rates of cancer and cancer-related health disparities. For example, Black or African American men have the highest cancer incidence rate in the United States, and both African American men and women have the highest death rate for most cancers compared with any other racial or ethnic group (75). In terms of gender or biological sex, the majority of co-users were male, and co-users were more likely to be male compared with both cannabis-only and tobacco-only users. Furthermore, from 2004 to 2012, co-use also increased at a faster rate among males than females (71). Lastly, high proportions of co-users reported low income (less than $20 000) and low educational attainment compared with marijuana-only and tobacco-only users. This disparity in co-use by socioeconomic status is particularly relevant to cancer risk because prior research shows that the mean cancer death rate is higher in the lowest-income counties in the United States (76).

Theories of Co-Use and Initiation

There are several theories that could explain co-use, and it is likely that no single theory predicts co-use. A review of all theories is beyond the scope of this article; however, the most relevant theories are briefly discussed. The gateway hypothesis (77) suggests that substance use follows a sequence starting with "low hanging fruit," such as alcohol or tobacco, and then progresses into "harder" drugs such as cannabis. Given that cannabis is legalized in some form in most of the United States, the gateway hypothesis may be less applicable to today's new initiates. The reverse gateway hypothesis, in contrast, may be more applicable. According to this theory, "harder" drugs, such as cannabis, precede "softer" drug use, such as alcohol or tobacco (78), perhaps as individuals mature out of harder drug use. According to the vulnerability hypothesis, co-use is a symptom or expression of an underlying vulnerability or predisposition to engage in a variety of health-risk behaviors (79), including cannabis use (among others). Reinforcement theories would suggest that cannabis is used to enhance the high of inhaled nicotine, such as with blunt smoking, or, conversely, that nicotine is used to counteract the dampening or depressing effects of cannabis, such as when one "chases" cannabis use with a cigarette (80,81). Finally, peer norms also likely play a strong role in co-use behavior. The effects of leaving home or going to college influence the co-use of a variety of substances that were previously forbidden or considered "off limits" when living at home. We see this exemplified in published research showing that cannabis and other substance use typically increases during the transition period from high school graduation and the first year of college (8,9).

The associations between tobacco and cannabis initiation are most likely reciprocal and dynamic, because the literature remains unclear about which product comes first. In some studies, tobacco use predicts the onset of cannabis use. For example, 1 recent study found that e-cigarette use predicts subsequent cannabis use among youth and young adults (82). In another national study using PATH data, youth and young adults who report a pleasant first–cigarette-smoking experience were more likely to report subsequent cannabis use, whereas those who reported an unpleasant first-cigarette experience were less likely to report subsequent cannabis use (83). In other studies, cannabis use has been shown to predict the onset of tobacco use among never users of a particular tobacco product. For example, in a national study of young adults, ever use of cannabis at baseline predicted the subsequent onset of LCC use, whereas baseline use of LCCs and large cigars did not predict the subsequent onset of cannabis use (84). Lastly, another study of a national sample of young adults found that some-days or everyday use of cannabis predicts hookah initiation in as little as 6 months. In this study, 22% of young adults who reported hookah trial 6 months after baseline reported "everyday" or "some-days" cannabis use at baseline (85). A more thorough review of the sequencing of cannabis initiation vis-à-vis tobacco is beyond the scope of the article.

Individual Tobacco Product Co-Use With Cannabis

Co-Use of Cannabis With Cigarettes

Cigarettes are the most popular tobacco product among co-users. One study, using data from the National Survey on Drug Use and Health, showed that 60% of past-month cannabis users reported current cigarette smoking (86), and another study from the PATH Study data showed that 30% of current cigarette smokers reported past-year cannabis use (87). Daily cannabis use has also increased specifically among cigarette smokers in the past decade (27). The most rapid increase of daily cannabis use has been found among former smokers (88), suggesting possible compensatory effects as former smokers may be using cannabis to attenuate withdrawal symptoms and substitute for the behavioral pattern of physically smoking a cigarette. Cannabis use among smokers is also linked to greater cannabis problem severity. For example, 1 US population-based study found that cannabis use disorder is 2 to 4 times more common

among cigarette smokers than nonsmokers (58). Chasing cannabis with tobacco is associated with greater cannabis dependence symptoms. Specifically, those who report a greater frequency of smoking a cigarette or cigar or cigarillo after smoking cannabis are 3 to 5 times more likely to report cannabis dependence symptoms (12).

Co-Use of Cannabis With Cigars

Cannabis and cigar product co-use (inclusive of large cigars, little cigars/filtered cigars, and cigarillos) has become increasingly popular (86). For example, 20.6% of past-30-day cannabis users currently use cigars and 42% report current use of blunts (86). Specific correlates of cannabis and cigar co-use include being male, African American, and young adult and currently using cigarettes, alcohol, and illicit drugs. Cigar use is associated with the same negative health outcomes as cigarette smoking, including increased cancer risk, coronary heart disease, and chronic obstructive pulmonary disease. Blunts are a specific type of cannabis and cigar co-use. Blunts are overwhelmingly used by young adults, and they are perceived as being less harmful or addictive than other tobacco products (89). Misclassification of blunt is also a concern, because some users do not consider it to be a cigar or tobacco product, leading to underestimates in surveillance surveys. Furthermore, classification has health consequences—even though the tobacco may be fully removed from a blunt, the cigar wrapper contains nicotine (67), thereby increasing the addiction potential. Indeed, studies show that blunt smoking is associated with greater cannabis problems, including tolerance (89,90).

Co-Use of Cannabis With Hookah or Waterpipe and Electronic Nicotine Delivery Devices

The prevalence of cannabis vaping (eg, combining cannabis within a vaping device) has increased statistically significantly among all younger age groups in just the past few years. Data from 2017-2019 from the Monitoring the Future Study show that, in 2019, 21.8% of young adults, 20.8% of 12th graders, and 7% of 8th graders reported past-year cannabis vaping. Furthermore, analysis of changes from 2017 to 2019 showed a 6% increase in cannabis vaping among young adults, a 7% increase among 12th graders, and a small but still statistically significant 2.6% increase among 8th graders. The increase in cannabis vaping may be 1 reason behind the public health epidemic called EVALI—e-cigarette or vaping product use-associated lung injury—which was largely driven by vitamin E acetate found in the THC oils being used in e-devices (more details about this are provided in the final section of this manuscript). Less is known about cannabis co-use with hookah. According to published PATH data, 51.7% of adult past-year hookah users reported past-year cannabis use, whereas only 10% of nonhookah users reported past-year cannabis use (87). Among youth, 65.5% of ever hookah users reported ever using cannabis compared with just 9.5% of never hookah users (91).

Conclusion

Although there are benefits from cannabis use for certain health conditions, some people may experience harms from use. The co-use of cannabis with tobacco is associated with a variety of health problems. Combustible tobacco use is particularly high among cannabis and tobacco co-users (co-users) relative to tobacco-only users. This is quite concerning because tobacco use is the leading cause of cancer. The co-use of cannabis with tobacco is especially common among demographic groups that have a higher cancer risk—Black or African American individuals, males, and individuals of low socioeconomic status (71,86,92,93). Continued co-use may place these subgroups of users, who often suffer disproportionately from tobacco-related diseases and mortality as they get older, at a higher risk for poor health outcomes. Unique co-use smoking practices, acute toxin exposure from co-use (ie, more carbon monoxide exposure than cigarettes) (74,94–96), and disproportionate use by vulnerable individuals with higher cancer risk justify why co-use merits increased research attention. Despite burgeoning research on cannabis and tobacco co-use patterns and correlates, the immediate (eg, acute) and longer-term health effects of exposure to co-use behavior are not fully known. This is unfortunate given the high prevalence of co-use among vulnerable groups that show high cancer risk and tobacco-related health disparities. Finally, it is important to note that cannabis industry and Big Tobacco industry practices outpace public health efforts to intervene on the health consequences associated with co-use and could be a key factor in shaping co-use in the future. The tobacco industry spends approximately $24 million per day in marketing and advertising, which is just over $9 billion per year (97). The cannabis industry was estimated to have spent approximately $6 million per day in 2019 on marketing, which was approximately $2.26 billion for that year (98). Statistically significant increases in public health funding would need to occur to counteract industry spending and messaging aimed at recruiting and retaining new consumers for the cannabis and tobacco markets.

Potentially Harmful Inhalational Exposures From Smoked and Vaped Cannabis

This section reviews the state of the science on harmful inhalational exposures related to smoked and vaped cannabis use. Specifically, potentially harmful exposures are documented through analytical measurements of product constituents and emissions as well as the biomarkers of exposure to toxicants and carcinogens in product users (99). This text describes potentially harmful chemicals in cannabis smoke (15); biomarkers of smoke exposure following controlled use of cannabis in joints, vapes, and edibles (100); population-based data for recent cannabis users (16) and for dual users of tobacco and cannabis (23); and lung injuries associated with the use of e-cigarette, or vaping, products (17).

Carcinogens and Toxicants in Cannabis Smoke

The potential harm caused by cannabis exposure can be assessed based on the analysis of chemicals to which users are exposed. Most notably, many of the same potentially harmful chemicals that form in tobacco smoke also form in cannabis smoke (15). Carcinogenic and toxic volatiles (eg, benzene, acrolein), polycyclic aromatic hydrocarbons (eg, naphthalene, pyrene), aromatic amines (eg, 4-aminobiphenyl, 2-aminonaphthalene), and carbon monoxide form in similar qualitative patterns and quantitative amounts per gram of product. These smoke toxicants account for much of the cancer and noncancer health risks of smoked tobacco (101,102), and similar hazard indices can be extrapolated for cannabis smoke. An important caveat is that the mass of cannabis smoked by daily cannabis smokers tends to be substantially less than the mass of tobacco smoked by a daily cigarette smoker, and thus smoke

exposure biomarkers tend to be lower in daily cannabis smokers compared with daily tobacco smokers (103).

The route of exposure to cannabis substantially affects exposure to harmful smoke chemicals. A recent study measured smoke exposure biomarkers in sequential urines collected from study participants following controlled use of cannabis in joints, vapes, and edibles (100). Smoking a single cannabis joint led to a substantial increase in exposure to carcinogenic acrylonitrile as assessed by measuring the urinary metabolite cyanoethyl mercapturic acid (a range of increase of 55% to 1570%). As expected, acrylonitrile exposure did not change in response to vaping or eating cannabis products (100). Thus, the route of exposure can statistically significantly impact the health risks associated with cannabis product use.

Several population-based studies have assessed the harmful exposures associated with smoking cannabis. The National Health and Nutrition Examination Survey includes the collection of both questionnaire data about cannabis and as urine samples. Cannabis use was broadly defined in National Health and Nutrition Examination Survey and did not specify a particular mode of administration (eg, edible, combusted). Multiple studies found that recent cannabis use is associated with increased exposure to polycyclic aromatic hydrocarbons, volatile organic chemicals, and cyanide compared with nonusers (16). Studies must control for tobacco smoke exposure so that smoke biomarker differences can be attributed exclusively to cannabis smoke exposure despite the common co-use of tobacco and cannabis (104). Furthermore, the same data were evaluated to show that more frequent cannabis use led to higher smoke exposure than did less frequent use (105). Smoke exposure was further explored with questionnaire and biomarker data collected as part of the PATH Study. Across all groups of tobacco users, those who co-used cannabis had higher exposure to carcinogenic acrylonitrile compared with noncannabis users (by 39%-464%). Tobacco-cannabis co-users also had statistically significantly higher levels of the biomarkers of exposure to acrylamide, fluorene, and pyrene compared with exclusive tobacco users (23), which is indicative of statistically significantly higher smoke exposure in co-users compared with exclusive users of either product.

Potential for Inhalational Harm From Vaped Cannabis

Electronic vaping products (EVPs) aerosolize e-liquid constituents without forming smoke and thus likely emit lower levels of carcinogens and toxicants compared with smoked products. However, EVPs are not without risks. E-liquids can contain harmful constituents, such as pesticides, solvent residues, and toxic metals from the original plant material or from processing and storage (106,107). Furthermore, harmful chemicals can form during product use when liquid is aerosolized (eg, formaldehyde and other carbonyls) (108), although typically at concentrations lower than that found in smoked product emissions.

EVPs continue to evolve around different uses; for example, a new class of EVPs use a ceramic heating element designed to more efficiently transfer oils, such as THC, to the aerosol phase (109). Other devices allow users to modify filament voltage and other settings. Such changes in design undoubtedly affect inhaled exposures resulting from use of cannabis vape products and thus warrant further research.

Over the last few years, EVP use of both nicotine and cannabis has increased substantially, especially in youth and young adults (110,111). This proliferation of EVPs increased the prevalence of vaping THC e-liquids from unregulated sources, such as websites and informal channels (112). These unregulated marketplaces for EVPs and THC vape liquids are thought to have contributed to an outbreak of EVALI in 2019-2020 (112). EVALI cases (N = 2807) were typically hospitalized with serious respiratory distress, and 68 deaths were reported across 29 states and Washington, DC (113). Those injured were more likely to be young adult, male, non-Hispanic White, generally healthy, and reporting e-cigarette use in the 3 months before symptom onset. The mean duration of hospitalization was 6 days, with most case patients requiring supplemental oxygen or mechanical ventilation (114). The evidence pointed to inhalational exposure to causal chemical(s); however, associating specific products with injury was difficult because vaping cartridges were not always available to test and case patients were not always fully forthcoming about their use of potentially illicit products.

The cause of the EVALI outbreak was identified based on measurement of a variety of potentially toxic additives (eg, plant oils, petroleum distillates, medium-chain triglycerides, terpenes, vitamin E acetate [VEA]) in residual bronchoalveolar lavage (BAL) fluid that had been collected from EVALI case patients (115,116). BAL fluid reflects the chemical composition of the lung epithelial lining fluid, and thus these new analytical methods could identify chemicals that were accumulating at the primary site of injury in EVALI case patients. Of the 51 BAL fluids tested, 48 (91%) contained measurable VEA; conversely, no other potential toxicants were widely detected. Furthermore, no VEA was detected in BAL fluid collected from 99 otherwise healthy comparators who were not using cannabis vape products (17). VEA is a shelf-stable form of vitamin E, which is used as a dietary supplement and in cosmetic products. VEA is generally recognized as safe when ingested; however, this chemical had not been evaluated adequately for inhalational toxicity. Multiple trade websites had reported the practice of diluting THC oil with VEA to reduce the production cost (117). Subsequent analysis of case-associated products also implicated VEA: EVALI cases typically reported using at least 1 product that contained VEA (118), and the presence of VEA in THC vape products confiscated by law enforcement correlated well with the EVALI outbreak (119,120). Importantly, mice exposed to vaped VEA developed lipid-laden macrophage and lung injury, consistent with VEA as the inhaled toxicant that caused the EVALI outbreak (121). Vaped VEA could plausibly cause lung injury through either directly disrupting surfactant action (122) or by decomposing to form reactive ethenone (123,124).

Conclusion

In conclusion, cannabis product use may result in increased exposure to harmful chemicals from either smoke or vape constituents. The potential harm caused by smoke inhalation is well characterized and warrants consideration in risk–benefit assessments related to cannabis. Additional research is needed to inform efforts to prevent future outbreaks related to vaped THC and to characterize the long-term impact of EVALI for individuals and populations (125). These efforts could include longitudinal studies of EVALI patients, characterization of EVALI case-associated product fluids and emissions, independent characterization of chemical constituents of cannabis products or emissions, and evaluation of the respiratory toxicities of inhaled emissions of common vape additives such as VEA (112).

Discussion and Future Directions

Enhancing existing public health research about cannabis use and related cancer or health risks is critical given the rapid changes in cannabis legalization across the United States, the putative links between cannabis use and cancer, the high co-occurrence of cannabis with tobacco use, and increased exposure to harmful chemicals from vaped and combusted cannabis use. Additional research is needed in all 3 areas covered to address challenges and gaps, including the role of public health, detection of harmful components correlated with cannabis use (eg, pesticides, heavy metals, mold), harm-reduction messaging, the potency of cannabis products, and changes in the federal laws about cannabis use.

Regulatory Science to Advise Public Health Policy

Regulatory science refers to measurement, assessment, modeling, and impact analysis studies that provide the empirical basis for informing and enacting policies and regulatory actions. Regulation of cannabis use in the United States varies from state to state and is often driven by factors such as public ballot initiatives that do not necessarily result in effective policy that protects public health. Policies are often developed rapidly, and typically post hoc, to keep pace with the rapidly changing legal cannabis landscape. Furthermore, little to no attention has been given to the potential downstream effects of local and state cannabis laws and policies on other behaviors and substances that have a high co-occurrence with cannabis use, including alcohol use and tobacco use (both of which are linked to increased cancer risk). The study of cannabis use provides a host of opportunities for public health stakeholders and researchers in academia and nonprofit organizations to work together to collaboratively collect data that will inform policy and examine the outcomes of new policies. Data monitoring and collection of cannabis trends, patterns, and correlates at the national, state, and local levels are also important and should occur in states before policies change so that the impact of policy changes can be examined. The public should be educated before policy changes so they know about the products, the science, and how policies affect use. Public health agencies need to engage with community members to create safe environments that reduce the risk of exposure to secondhand cannabis smoke.

Detection of Pesticides, Heavy Metals, and Mold Exposures Related to Cannabis Use

None of the epidemiological studies reviewed have considered pesticides, heavy metals, solvents, adulterants, or mold exposures associated with cannabis use. It will be important to conduct laboratory studies to characterize what happens to pesticides during the smoking or vaping process and understand the potentially harmful exposure from such product constituents in conjunction with cannabis inhalation or cannabis use. From a policy perspective, few states are currently testing for the breadth of heavy metals in cannabis products, and developing testing methods across products has been challenging. Research in this area would be important for consumers so they are aware of the additional chemicals they may be ingesting or inhaling when they use cannabis.

Harm-Reduction Messaging

There was a discussion at the end of the session between symposium participants and the symposium co-chairs that states with legal cannabis marketplaces are beginning to see messaging focused on harm-reduction techniques from cannabis use, rather than abstinence all together, such as “Start low, go slow.” Edible dosing policies in states with legalization are meant to set lower doses to prevent overconsumption. Harm-reduction messages could be evaluated in research studies, although to date, most evaluations have been left to state or local health departments. Given the high rates of cannabis co-use with tobacco and potential links between cannabis use and increased cancer risk, improving cannabis prevention program effectiveness, particularly targeting younger users, will have substantial positive public health impacts. Given that cannabis is now legal in a number of states, we need to think about what messages can promote responsible use among adults while also deterring initiation and uptake among younger users. Careful attention should be given to how low levels of use are defined, because most recent research focuses on correlates and consequences associated with daily or near daily use. However, understanding the potential benefits with respect to the harms associated with low levels of use is important for informing policies because the benefits may outweigh the risks. For example, the National Institute on Alcohol Abuse and Alcoholism has set forth recommended guidelines for consuming alcohol at nonrisky levels (no more than 1 drink per day for women, and no more than 2 drinks per day for men). As yet, no recommended broad guidelines exist for cannabis use, nor are there specific guidelines for individual routes of administration (eg, edibles, lotions, concentrates, oils).

Public health messaging campaigns (deployed via print, radio, television, web, or mobile platforms) are well suited for disseminating information about cannabis health risks to a large and diverse audience to effect behavior change; however, the rapid enactment of marijuana legalization policies and increased pressure from the general public to ease restrictions nationwide have outpaced efforts to devise and disseminate prevention programs using rigorous scientific approaches that are relevant to the current marijuana policy landscape. The statistically significant increases in cannabis use and its co-use with tobacco, as well as the concomitant decline in cannabis harm perceptions across all age groups over the past decade, indicate that current public health campaigns have not been effective at correcting misperceptions about cannabis-related harm and that more work in this area needs to be done.

Potency of Cannabis Products, Modes of Cannabis Administration, and Duration of Use

There is wide variation in the potency and quality control of cannabis products, modes of administration, duration of use, and dosing recommendations (in medically legal states), which all have implications for cannabis dependence, how dependence on cannabis may affect co-use behaviors and other health consequences, and the ability to quit using cannabis. Because the vast majority of research on cannabis potency has been on plant-based smoked cannabis, it is difficult to make conclusions about the long-term health effects of current types of cannabis use beyond loose-leaf cannabis. The compendium of research thus far indicates that current cannabis potency has increased in the United States over the last 2 decades (126). It

will be important to understand the extent to which cannabis potency may interact with different forms of tobacco product consumption (eg, cigarette smoking vs electronic vaping device use) to affect the risk of cancer and tobacco-related disease. We may expect an increase in dependence because there are more potent products that are being consumed at daily or near daily levels, and the more individuals consume, the higher the association with dependence. In manufacturing these concentrations, there are other public health implications, such as the health and safety of the workers employed at cannabis-growing facilities and farms, inaccurate labeling of potency, and unanticipated poisoning. States vary with respect to product testing and regulation policies, and thus variation in public health impact could be due to state-level regulations.

In terms of modes of administration, large epidemiological studies are now just beginning to examine the correlates and possible health consequences of tobacco co-use with different modes of cannabis ingestion beyond combustible cannabis use (eg, edibles, oils, concentrates). Several US population-based surveys, such as the PATH Study, the National Survey of Drug Use and Health, and the Behavioral Risk Factor Surveillance System, have recently included new questions to assess a variety of cannabis modes of delivery. Analysis of these data will allow us to assess, from a broader perspective, how modes of cannabis delivery are changing over time (alone and in conjunction with tobacco product), the frequency and duration of these modes of use, and whether the frequency and duration of emerging cannabis modes of administration have positive health benefits (eg, by substituting other forms of tobacco use) or negative health benefits (by interacting with other forms of tobacco use).

Need for Cannabis Research

With the proliferation of legalized, medical, and decriminalized cannabis in the United States, concerns have been raised that greater availability could lead to increased incidence of poor health outcomes associated with cannabis use, such as co-use with tobacco and increased cancer risk. Currently, because of the Schedule I classification of cannabis at the federal level, researchers who do not possess a Schedule I license to conduct research are unable to examine cannabis health effects under controlled conditions. Obtaining a Schedule I license is financially costly and requires personnel effort to ensure that studies adhere to a plethora of regulatory guidelines. To improve our understanding of the association of nonmedical cannabis use with cancer and cancer-related behaviors and outcomes, there are a number of issues regarding the acute and long-term health effects of cannabis use that could be easier to study if Schedule I obstacles were addressed. These issues include, but are not limited to 1) understanding the influence of cannabis on cancer symptom management in clinical trials; 2) measuring the health impacts, such as cell damage and cytotoxicity in humans, in response to controlled use of different forms of cannabis at various dosages of THC and cannabidiol; and 3) quantifying the exposure, toxicity, and carcinogenic impact of different patterns of cannabis smoking using laboratory smoking topography paradigms that measure how combusted products are smoked (eg, number of puffs taken, interval between puffs, puff volume). Anecdotally, researchers and their institutions are hesitant to examine cannabis use, even in basic survey studies, because it is illegal at the federal level. This places a tension between the need to understand more about the correlates and health consequences of cannabis use and the need to abide by federal laws. Although some institutions across the United States have received approvals to conduct cannabis administration studies, with a Schedule I license, obtaining such privileges is costly and time-consuming.

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Data Availability

This monograph used publicly available data from the Population Assessment of Tobacco and Health (PATH) study.

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